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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/479,783	01/07/2000	STANLEY T CROOKE	ISIS-4313	3541
34138	7590	02/09/2005	EXAMINER	
COZEN O'CONNOR, P.C. 1900 MARKET STREET PHILADELPHIA, PA 19103-3508			MCGARRY, SEAN	
			ART UNIT	PAPER NUMBER
			1635	

DATE MAILED: 02/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/479,783

Applicant(s)

CROOKE, STANLEY T

Examiner

Sean R McGarry

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 21 November 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 78-81,93-102,106 and 117-181 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 78-81,93-102,106 and 117-181 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>9/20/04</u> . | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 78-81, 93-102 and 106 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection has been withdrawn in view of applicants amendments filed 11/21/04.

Claims 78-81, 93-102, 106 remain and new claims 117-181 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is maintained for the reasons of record.

The claimed invention is based on the substrate for a dsRNAse from T24 cells. The structure of the dsRNAse has not been disclosed. The claimed invention is drawn to a "double stranded RNA substrate". The scope of the claimed invention is vastly wider than a substrate for a particular dsRNAse, for example. The specification, as filed describes particular 2' methoxy modifications with RNA gaps (See Figure 1, for example) that allowed the function of acting as a substrate for the RNAse from T24 cells. The scope of substrates disclosed in the instant specification is therefore narrow.

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The claimed invention is drawn to dsRNA substrates with modifications that provide for increased hybridization and/or increased nuclease stability while allowing the dsRNA substrate to act as a "substrate". It is noted that no other substrate function other than the specific dsRNase substrate function has been disclosed in the instant specification. It is noted that the specification does not, for example, indicate any particular functional characteristics [substrate functions, for example] that are coupled with a known or disclosed correlation between function and structure. The specification does not disclose the structure of the specific dsRNase used to determine the functionality of the specific substrate disclosed in the instant specification for example. As is noted in the instant specification, RNase H is very sensitive to structural alterations in antisense oligonucleotides (see page 2, for example). There is no indication that dsRNases as a class would be non-effected by chemical modifications, for example. The instant invention, for example, reads on double stranded RNA substrates for any dsRNase protein. The instant specification provides no structure function relationship for any of these potential dsRNases and any particular modification that may or may not allow a dsRNA to function as a substrate for any particular dsRNase. Furthermore, it is not so clearly described what the function of substrate may be, for example. The instant specification describes a specific RNases that acts to cleave a substrate. The instant claims are not so limited but embraces any conceivable function of a substrate, for example. To satisfy the written description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in

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the art would recognize that the inventor possessed the claimed invention at the time of filing. *Vas-Cath*, 935 F.3d at 1563.

Applicant's arguments filed 11/21/04 have been fully considered but they are not persuasive. Applicant argues that since the terms "double stranded RNA substrate" has been deleted from the claims, the invention is now described. It is unclear how the amendment provides for a description of the invention since the disclosed invention of the application is in fact a double stranded RNA that is cleaved by a dsRNase. The specification discloses single stranded RNA targeted to target RNAs to be cleaved by an dsRNase. At pages 93 it is disclosed double stranded RNAs that were used in cell lysates to detect dsRNase activity. The amendment fails to provide a description or provide a scope of the disclosed invention that has been adequately described. The scope of the invention has not been narrowed by the amendments but appears to have broadened the scope, for example (see applicants response, page 13, last sentence of third paragraph). For example, the amendments to the claims make it clear that the invention is now not limited to "RNA-like" oligomers as described in the specification as filed. The rejection is maintained for the reasons of record. Applicants' response fails to specifically address the reasons provided for finding a lack of adequate written description in the rejection of record.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 96, 98, 99, and 100, remain and new claims 142, 144-146, 154, 156-158, 160, 162-164, 166, and 168-170 are rejected under 35 U.S.C. 102(b) as being anticipated by Ohtsuka et al [US 5,013,830, cited by applicant].

Ohtsuka et al have disclosed in Table 5 and the claims, for example double stranded oligonucleotides that comprise double stranded RNA portions. The compounds include one oligonucleotide that comprises both DNA and RNA portions. The RNA/DNA oligonucleotide hybridizes to an RNA oligonucleotide. Since RNA:RNA hybridizations are stronger than RNA:DNA hybridizations one can reasonably interpret such modification to be a modification that increases the affinity of an oligonucleotide [all DNA as opposed to RNS/DNA, for example] to a complementary oligoribonucleotide. The compound also includes the 2'-O-Me modifications which increase resistance to nucleases which are required by the instant claims. It is noted that the claims as amended do not require an RNA portion.

Applicant's arguments filed 11/21/04 have been fully considered but they are not persuasive. Applicant argues that the definition of "modification" of the specification is inconsistent with that used by the examiner. A review of the specification failed to yield a specific definition of the term "chemical modification". If applicant believes that there is

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such a definition applicant is invited to point to such with particularity. Otherwise the argument is moot. It is noted that the "RNA basis" of the rejection is not required to maintain the rejection since the limitations are otherwise met. Applicant argues that the amendment to the claims drawn to "eight to fifty renders the invention novel since applicant asserts that the oligomer or Ohtsuka contains a strand of at least 90mer. It is noted that the claims require that the strands comprises 8-50. 90 comprises 8-50. The rejection is maintained.

Claims 78, 94, 95, 99, and 101 remain rejected under 35 U.S.C. 102(b) as being anticipated by Froehler et al [US 5,256,775, cited by applicant].

Froehler et al disclose RNA oligonucleotides (see column 4, for example) that are 3-50 nucleotides in length which contain modification on the 3' and 5' ends to protect from nucleases where the central portion of the oligonucleotide is phosphodiester linked (see column 5, for example). Since these oligonucleotides are disclosed for use to hybridize and inhibit an RNA target such as mRNA (see column 1 and 12, for example), the instantly claimed invention has been disclosed.

Applicant's arguments filed 11/21/04 have been fully considered but they are not persuasive. Applicant argues that the amendment to the claims drawn to "eight to fifty renders the invention novel since applicant asserts that the target in the invention of

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Froehler et al is an mRNA and would thus be longer than 50. It is noted that something longer than 50 would comprise 50, for example.

Claims 96, 98, 99, 100, 143, 155, 161, 167 are rejected under 35 U.S.C. 102(b) as being anticipated by Ohtsuka et al [Journal of Biochemistry, Vol. 139:447-450, 1984, cited by applicant on form 1449, filed 9/20/04].

Ohtsuka et al disclose cleavage of a ds8mers that comprise 2'flouro modifications.

Claims 78, 80, 81, 93-96, 98-102, 117-122, 129-146 and 153-175 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. All of the above claims have been amended to or depend from claims that have been amended to read on double stranded oligomers where both strands comprise 8-50 nucleotides. Applicant points to page 7, lines 13-16 of the specification for support. Page 7 does indeed contain the words "eight to fifty" but not in the context now used. At page 7 of the specification the discussion is drawn to a single stranded RNA-like oligomer that is used to bind a target RNA. The target RNA is not discussed as being 8-50 nucleotides in length. The examiner was unable to find clearly apparent support for such a limitation in the context now used from the specification or claims as

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originally filed. If applicant believes that such support exists they are invited to point to such support with particularity.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action and further applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 9/20/04 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See See MPEP § 706.07(a) and MPEP § 609(B)(2)(i). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

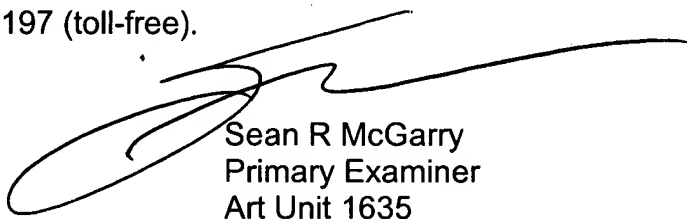
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean R McGarry whose telephone number is (571) 272-0761. The examiner can normally be reached on M-Th (6:00-4:30).

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Sean R McGarry  
Primary Examiner  
Art Unit 1635

SRM